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=> s (il-6 (a) receptor) (a) antibody (p lymphocyte

L1 46 IL-6 (A) RECEPTOR (A) ANTIBODY (P) LYMPHOCYTE

dup rem 11

PROCESSING COMPLETED FOR L1
L1 26 DUF REM L1 (26 DUPLICATES REMOVED)

=> s (il-6 (a) receptor) (a) antibody (p lymphocyte and human?

3 FILES SEARCHED...

L3 33 IL-6 (A) RECEPTOR (A) ANTIBODY (P) LYMPHOCYTE AND HUMAN?

dup rem 13

PROCESSING COMPLETED FOR L3
L3 16 DUP REM L3 (17 DUPLICATES REMOVED)

=> d 14 total kbib kwic

L4 ANSWER 1 OF 16 USPATFULL

ACCESSION NUMBER: 2000:117820 USPATFULL
TITLE: G-protein coupled receptor protein and a cDNA encoding the receptor
INVENTOR(S): Hiruma, Shuji, Tsukuba, Japan
Hosoya, Masaki, Tsuchiura, Japan
Fujii, Eyo, Tsukuba, Japan
Ohtaki, Tetsuya, Tsukuba, Japan
Fukusumi, Shoji, Tsukuba, Japan
Ohgi, Kazuhiko, Tsukuba, Japan
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Osaka, Japan
(non-U.S. corporation)

| | NUMBER | DATE |
|---------------------|----------------|--------------------------|
| PATENT INFORMATION: | US 6114139 | 20000905 |
| | WO 9505342 | 19960222 |
| APPLICATION INFO: | US 1995-011974 | 19950914 (8) |
| | WO 1995-JP1599 | 19950310 |
| | | 19950914 PCT 371 date |
| | | 19950914 PCT 102(e) date |

| | NUMBER | DATE |
|--|---|----------|
| PRIORITY INFORMATION: | JP 1994-184272 | 19940811 |
| | JP 1994-184273 | 19940811 |
| | JP 1994-184274 | 19940811 |
| | JP 1994-184275 | 19940811 |
| | JP 1994-184276 | 19940811 |
| | JP 1994-184277 | 19940811 |
| | JP 1994-184278 | 19940811 |
| | JP 1994-184279 | 19940811 |
| | JP 1994-184280 | 19940811 |
| | JP 1994-184281 | 19940811 |
| | JP 1994-184282 | 19940811 |
| | JP 1994-184283 | 19940811 |
| | JP 1994-184284 | 19940811 |
| | JP 1994-184285 | 19940811 |
| | JP 1994-184286 | 19940811 |
| | JP 1994-184287 | 19940811 |
| | JP 1994-184288 | 19940811 |
| | JP 1994-184289 | 19940811 |
| | JP 1994-184290 | 19940811 |
| DOCUMENT TYPE: | Utility | |
| PRIMARY EXAMINER: | Walsby, Stephen | |
| ASSISTANT EXAMINER: | Park, Michael D. | |
| LEGAL REPRESENTATIVE: | Conrad, David G.; Resnick, David S.; Dike, Bronstein, Robert & Cushman, LLP | |
| NUMBER OF CLAIMS: | 6 | |
| EXEMPLARY CLAIM: | 1 | |
| NUMBER OF DRAWINGS: | 73 Drawing Figure(s); 81 Drawing Page(s) | |
| LINE COUNT: | 11014 | |
| CAS INDEXING IS AVAILABLE FOR THIS PATENT. | | |

L4 ANSWER 2 OF 16 USPTAFULL

ACCESSION NUMBER: 100000580 USPTAFULL

TITLE: Nucleic acid construct for expressing active substances

which can be activated by proteases, and preparation and use

INVENTORS : Heidmann, Hans Heinrich, Marburg, Germany, Federal Republic of
Mueller, Rolf, Marburg, Germany, Federal Republic of
Sedlaeck, Hans-Harald, Marburg, Germany, Federal Republic of

PATENT ASSIGNEE(S): Hoechst Aktiengesellschaft AG, Germany, Federal Republic of (non-U.S. corporation)

| | NUMBER | DATE |
|---------------------|--------------|--------------|
| PATENT INFORMATION: | US 6080575 | 20000627 |
| APPLICATION INFO: | US 1998-0308 | 19980116 (9) |

| | NUMBER | DATE |
|--|--|----------|
| PRIORITY INFORMATION: | DE 1997-19701141 | 19970116 |
| DOCUMENT TYPE: | Utility | |
| PRIMARY EXAMINER: | Harrell, Paula K. | |
| ASSISTANT EXAMINER: | Sun-Hoffman, Lin | |
| LEGAL REPRESENTATIVE: | Foley & Lerner | |
| NUMBER OF CLAIMS: | 22 | |
| EXEMPLARY CLAIM: | 1 | |
| NUMBER OF DRAWINGS: | 3 Drawing Figure(s); 3 Drawing Page(s) | |
| LINE COUNT: | 2578 | |
| CAS INDEXING IS AVAILABLE FOR THIS PATENT. | | |

DETL Examples of promoters and activator sequences which are activated in lymphocytes and/or macrophages are the promoter and activator

sequences of the gene encoding cytokines, cytokine receptors and adhesion molecules, and receptors for the Fc fragment of **antibodies**. Examples of these are: IL-1 receptor, IL-1.alpha., IL-1.beta., IL-2, IL-2 receptor, IL-3, IL-3 receptor (.alpha. subunit), IL-3 receptor (.beta. subunit), IL-4, IL-4 receptor, IL-5, IL-6, **IL-6 receptor**, interferon regulatory factor 1 (IRF-1, [the promoter of IRF-1 is activated to the same extent by IL-6 as by IFN.gamma. . . .

DETD an antibody molecule or the epitope-binding moiety of an antibody molecule. The murine monoclonal antibodies should preferably be employed in **humanized** form. The **humanization** is effected in the manner described by Winter et al. Nature 349, 293 (1991) and Hopp et al. Rev. Imm. . . .

DETD Recombinant antibody fragments are either prepared directly from existing hybridomas or are isolated from libraries of murine or **human** antibody fragments [Winter et al., Annu. Rev. Immunol. 12, 433 (1994)] using the phage-display technique [Smith, Science 266, 1315 (1994),

DETD also be used to isolate new antibody fragments directly from antibody libraries [immune libraries or naive libraries] of murine or **human** origin. In the phage-display of antibody fragments, the antigen-binding domains are cloned, as protein fusions with the coat protein p8. . . .

DETD which are specific for human [Orlandi et al., PNAS-U.S.A., 86, 3853 (1989), Sastry et al., PNAS-U.S.A., 86, 5728 (1989)] or **human** immunoglobulin genes [Barrick et al., BREC 150, 1250 (1989) or for the **human** immunoglobulin gene families [Marks et al., Eur. J. Immunol. 21, 485 (1991)].

DETD reselecting under stringent conditions [Hawkins et al., J. Mol. Biol. 197, 489 (1987)]. In addition, murine antibody fragments can be **humanized** by a stepwise replacement of one of the variable domains with a **human** repertoire and then selecting with the original antigen [guided selection] [Caspers et al., Bio/Technol. 12, 889 (1994)]. Alternatively, murine antibodies are **humanized** by specifically replacing the hypervariable regions of **human** antibodies with the corresponding regions of the original murine antibody [Jones et al., Nature 321, 512 (1986)].

DETD anchoring peptides include the transmembrane domains of cell membrane-located receptors or of viral proteins, such as the transmembrane sequence of **human** macrophage colony-stimulating factor (DNA p815 to ntoreq.1485 to ntoreq.1554; Cosman et al., Behring Inst. Mitt. 83, 18 (1988)] or the DNA sequence for the signal and transmembrane regions of **human** respiratory syncytial virus (RSV) glycoprotein G [amino acids 1 to 63 or their part sequences, amino acids 38 to 48;

DETD Fc gamma receptors of immune cells [Rojanasakul et al., Pharm. Res. 11, 171 (1994)]. They furthermore include the Fc fragment of **human** monoclonal or polyclonal immunoglobulin.

DETD which activate the complement cascade, for example cobra venom factor (CVF) or part sequences of CVF which correspond functionally to **human** complement factor C3b, i.e. which are able to bind to complement factor a and which, after having been cleaved by. . . . for CVF and its part sequences were described by Fritzing et al., Proc. Natl. Acad. Sci. U.S.A. 81, 12571 (1994), **human** complement factor C1b (the DNA sequence for C3 and its part sequences were published by De Fruyn et al., Proc. Natl. Acad. Sci. U.S.A. 82, 708 (1985), cleavage products of **human** complement factor C3 which resemble CVF functionally and structurally (such cleavage products have been described by O'Feeffe et al., J. . . .

DETD be a cytostatic, cytotoxic or inflammation-eliciting protein,

such as perforin, granzyme, cytokines, such as IL-1, IL-2, IL-4, IL-12, IL-3, IL-5, **human** leukemia inhibitory factor (LIF), IL-7, IL-11, IL-13, GM-CSF, B-CSF or M-CSF, interferons, such as IFN.alpha., IFN.beta. or IFN.gamma., INF, such as . . .

DETD . . . the active substance itself. Examples of such active compounds are bacterial nitroreductase, bacterial .beta.-glucuronidase, plant .beta.-glucuronidase derived from Setaria cereals, **human** .beta.-glucuronidase, **human** carboxypeptidase (CB), e.g. mast cell CB-A or pancreas CB-B, or bacterial carboxypeptidase, bacterial .beta.-lactamase, bacterial cytosine deaminase, **human** catalase or peroxidase, phosphatase, in particular **human** alkaline phosphatase or **human** acid prostatic phosphatase, type 5 acid phosphatase, oxidase, in particular **human** lysyl oxidase or **human** acid D-aminooxidase, peroxidase, in particular **human** glutathione peroxidase, **human** eosinophilic peroxidase or **human** thyroid peroxidase.

DETD . . . peptide, preferably, however, of nucleic acid sequences which encode those part structures D which naturally occur in the precursors of **human** active compounds.

DETD . . . *id.*, Mol. Cell Biol. 10, 2738 (1990); Herling et al., Cancer Res. 50, 5634 (1990) or the signal sequence of **human** respiratory syncytial virus glycoproteins [cDNA of amino acids.100eq.33 to 100eq.50 or 48 to 55; Lichtenstein et al., J. Gen. Virol. . . .

DETD . . . sequence.100eq.55 to 100eq.107; Rieckmann et al., Nature 342, 323 (1988)], is fused to component (b)(d), which contains the cDNA for **human** FX [nucleotide sequence 1 to 100eq.1468] [Messier et al., Gene 99, 291 (1991)] in which amino acid 194 has been . . .

DETD 1. Expression in **Human** Embryonic Kidney Cells

DETD Proliferating **human** embryonic kidney cells [HEK 293; Racchi et al., J. Biol. Chem. 268, 5735 (1993)] which are being maintained in culture. . . .

DETD In this test, the coagulation defect in **human** FX-deficient plasma is counterbalanced by functionally active FXa.

DETD 3. Expression in **Human** Endothelial Cells

DETD **Human** umbilical cord endothelial cells which are being maintained in culture are transfected with the above-described plasmid using the method known. . . .

14 ANSWER 3 OF 15 USPATFULL

ACCESSION NUMBER: 2000:4639 USPATFULL

TITLE: Modified protein for gene transfer and process for producing the same

INVENTOR(S): Takahara, Yoshiyuki, Kawasaki, Japan
Yanada, Naoyuki, Kawasaki, Japan
Notoh, Naoto, Kawasaki, Japan

PATENT ASSIGNMENT(S): Ajinomoto Co., Inc., Tokyo, Japan (non-U.S. corporation)
Drug Delivery System Institute, Ltd., Tokyo, Japan (non-U.S. corporation)

| | NUMBER | DATE |
|-----------------------|--|--------------|
| PATENT INFORMATION: | US 6013516 | 20000111 |
| APPLICATION INFO.: | US 1997-927087 | 19970910 (8) |
| RELATED APPLN. INFO.: | Continuation of Ser. No. US 1995-536280, filed on 29 Sep 1995, now abandoned | |

| | NUMBER | DATE |
|-----------------------|---|----------|
| PRIORITY INFORMATION: | JP 1994-270102 | 19940929 |
| DOCUMENT TYPE: | Utility | |
| PRIMARY EXAMINER: | Frieke, Scott D. | |
| ASSISTANT EXAMINER: | Nguyen, Dave Trong | |
| LEGAL REPRESENTATIVE: | Oblon, Spivak, McClelland, Maier & Neustadt, P.C. | |
| NUMBER OF CLAIMS: | 10 | |

EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Figure(s); 4 Drawing Page(s)
LINE COUNT: 698

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM 1. A biologically active peptide or protein which can be bound to a
specific receptor of a cell in a **human** body, and
SUMM 2. . . . and can transfer a nucleic acid into a specific type of cells,
a specific organ or tumor cells of the **human** body.
SUMM When a nucleic acid is administered to the **human** body for gene
therapy two difficulties arise. First, the nucleic acid is rapidly
decomposed. Second, the DNA cannot easily enter. . . .
DETD (8) **Human** red blood cells transglutaminase: Brenner et al,
Biochem. Biophys. Acta. 521, 4-13 (1978).
DETD 1.1 The substance shall not be retained at any site in the circulatory
system of the **human** body.
DETD 1.2 The substance shall not harm the **human** body.
DETD 1.3 . . . known examples include biologically active peptides obtained
in the nature, for example, peptides which exhibit a physiological
action in the **human** body, such as interleukin (IL -1, -2, -3,
-4, -5, -6, -7, -8, -9, -10, -11 and -12, G-CSF, GM-CSF, . . .
DETD Antibodies are also biologically active peptides within the context of
the present invention. Antibodies include not only **human**
monoclonal antibodies but also animal monoclonal antibodies. Most of
the

biologically active peptides must specifically bind to their
corresponding receptor. . . .
DETD 1.4 In chronic rheumatism, a **lymphocyte** that expresses an
IL-6 receptor is locally present and
precipitates production of an auto-**antibody**, which leads to an
attack or the progression of the disease.
DETD 1.5 . . . limited to polypeptides. Any substance which is available and
has
some affinity for DNA, which is not harmful to the **human** body
and which is not easily trapped in the circulatory system can be used.
DETD 1.6 . . . to stand at room temperature for 30 minutes. To the mixed
solution were added 1 ml of recombinant **human** IL-6
solution (2 ml of 10 mM sodium citrate, pH 7.0). The mixture was
mixed, and then allowed to stand. . . .

14 ANSWER 4 OF 16 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2000453012 MEDLINE
DOCUMENT NUMBER: 10345314
TITLE: Increased T-lymphocyte interleukin-6 binding in patients
with multiple sclerosis.
AUTHOR: Bengioanni P; Mosti S; Romano M R; Lombardo F; Moscato G;
Henrici O
CORPORATE SOURCE: Department of Neurosciences, Section of Neurology; and
Institute of Clinical Medicine, University of Pisa,
Italy..
bengioannissupl.1
SOURCE: Eur J Neurol, (2000 May) 7 (3) 291-7.
Journal code: DAF. ISSN: 1351-5101.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article: (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200010
ENTRY WEEK: 20001004
AB . . . nervous system associated with altered immunoregulation.
Interleukin (IL)-6 is a cytokine that has several effects on the
neuroimmune system. Specific **IL-6 receptors**
have been found in **human lymphocytes** and neuroglial
cells. The aim of the present study was to assay IL-6 binding on
peripheral blood T **lymphocytes** in MS patients. We found that T
cells from MS patients had significantly more **IL-6**
receptors [Bmax: 279 +/- 7 vs. 246 +/- 8 (mean +/- SEM)]

receptors/cell, in patients and controls, respectively], whereas Kd values. . . 9 vs. 300 +/- 12 (mean +/- SEM) receptors/cell, respectively). We found significantly (P < 0. 001) higher amounts of **IL-6 receptors** on CD4+ T cells from MS patients than on CD4+ **lymphocytes** from controls (484 +/- 11 vs. 363 +/- 11; (mean +/- SEM) receptors/cell, respectively; CD8+ T cells showed very few **IL-6 receptors** in both patients and controls. These data are discussed in terms of MS immune pathogenesis and pathophysiology, because T-cell activation seems to be linked to increased IL-6 binding. The upregulated IL-6 system might be involved in **antibody-mediated** demyelinating pathways, because IL-6 is well known to enhance humoral immune response.

CT Check Tags: Female; Human; Male
 Adolescence
 Adult
 CD4-CD8 Ratio
 CD4-Positive T-Lymphocytes: ME, metabolism
 Interleukin-2: BL, blood
 *Interleukin-6: ME, metabolism
 Middle Age
 Multiple Sclerosis: BL, . . .

L4 ANSWER 5 OF 16 USPATEFULL

ACCESSION NUMBER: 1998:44-3 USPATEFULL
 TITLE: Diagnos. and treatment of cancer having clonal macrophage involvement
 INVENTOR(S): McGrath, Michael S., Burlingame, CA, United States
 Herndler, Brian, San Francisco, CA, United States
 Shiramizu, Bruce, Pacifica, CA, United States
 PATENT ASSIGNEE(S): University of California, San Francisco, San Francisco, CA, United States (U.S. corporation)

| | NUMBER | DATE |
|-----------------------|---|--------------|
| PATENT INFORMATION: | US 5544122 | 19980428 |
| APPLICATION INFO.: | US 1996-001463 | 19960215 (8) |
| RELATED APPL. INFO.: | Division of Ser. No. US 1994-236745, filed on 5 Aug 1994, now patented, Pat. No. US 5580713 | |
| DOCUMENT TYPE: | Utility | |
| PRIMARY EXAMINER: | Chambers, Jasmine C. | |
| ASSISTANT EXAMINER: | Schruock, Jill D. | |
| LEGAL REPRESENTATIVE: | 2ret Field Bozicevic & Reed LLP; Bozicevic, Karl | |
| NUMBER OF CLAIMS: | 5 | |
| EXEMPLARY CLAIM: | 1,5 | |
| NUMBER OF DRAWINGS: | 1 Drawing Figure(s); 1 Drawing Page(s) | |
| LINE COUNT: | 1189 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM The title of the invention relates to cancer therapy; **human** immunodeficiency virus; recombinant macrophage; methods of diagnosis of macrophage involvement in cancer development; kits for use in diagnosis; and. . .

SUMM . . . in the cancer record, the macrophage is substantially eliminated from the cancerous tissue by administering to the mammal (preferably a **human**) harboring the cancerous tissue, a therapeutic agent that is in a formulation for preferential uptake by a macrophage. The administering. . .

SUMM . . . germ inhibitor, and gelonin (Kuejun) (Lifson, J. D., et al., supra). Trichosanthrin and monocharin inhibit expression of HIV antigens

in **human** blood cells including macrophages (Lifson, J. D., et al., supra).

SUMM . . . targeting moiety can be linked to a drug either directly or indirectly by carrier molecules such as serum albumin (particularly **human** serum albumin, polyanionic acids, dextran, and the like, by methods well known to those skilled in the art. The use of. . .

SUMM . . . means an oncogene which increases the probability of the

development of neoplasms (particularly malignant tumors) in a mammal (particularly a **human**). A gene associated with cell proliferation also includes a cell growth suppressing gene such that decreased gene expression of a . . .

SUMM By "HIV" is meant a **human** immunodeficiency virus of strains HIV-1, HIV-2, or other variants.

SUMM . . . of the invention are preferably designed for the diagnosis and treatment of clinical HIV- and non-HIV-associated macrophage-induced cancer in a **human**.

DETD . . . and hematopoietic (Akira, M. et al., Immunol Review (1992) 137:25-50). Many cell types, including monocyte/macrophages, fibroblasts, endothelial, B and T **lymphocytes**, chondrocytes, astrocytes and dentarytes are capable of producing IL-6. IL-6 can exert growth-inhibiting, growth-inhibitory or differentiation inducing activities depending upon. . . cells. In regard to lymphocytic stimulation IL-6 has been shown to be involved in 1) terminal differentiation of B-cells into **antibody** producing plasma cells; 2) induction of IL-2 and IL-3 receptors and differentiation of T-cells; and 3) IL-6 has been shown. . . of myeloma and hybridoma cells. Woodruff, G., et al., DNA and Cell Biology (1992) 11:587-592). IL-6 may cause transformation of **IL-6 receptor** expressing cells. Tonyama, H., et al., J Exp Med (1990) 171:589). IL-6 producing macrophages and epithelial cells were shown to. . .

DETD . . . invention involves probing the restriction digested and gel separated DNA with nucleic acid probes that hybridize to specific mammalian (preferably, **human**) genomic DNA regions.

DETD SMD mice are infected with **human** splenic tissue containing clonal HIV-infected macrophages. e.g., tissue from Case 100. Control SMD mice are infected with normal. . . HIV.

CLM What is claimed is:

. . . of a macrophage in vivo, said method comprising: a) injecting the macrophage of claim 1 into a tissue of a non-**human** mammal; b) growing said macrophage in said mammal until a tumor is present; c) administering to said mammal said candidate. . .

14 ANNOTATED COPY OF 16 MEELINE DUBLICATE 2

ACCESSION NUMBER: 18-113231- MEELINE

DOCUMENT NUMBER: 88-11313

TITLE: Mechanisms of growth control of Kaposi's sarcoma-associated herpes virus-associated primary effusion lymphoma cells.

AUTHOR: Asan H; Saba J W; Yang R; Munber R; Park D J; Kamada N; Koeffler H P

CORPORATE SOURCE: Division of Hematology Oncology and Pathology, Cedars-Sinai Medical Center, UCLA School of Medicine, Los Angeles, CA 90048, USA.

CONTRACT NUMBER: JG1 CA 6600-02 (NCI); CA 42710 (NCI)

SOURCE: BLOOD, 199- Apr 1) 81 (7) 2475-81. Journal code: ASG. ISSN: 0006-4971.

PUB. COUNTRY: United States

LANGUAGE: English

FILE SEGMENT: Abstracted Index Medicus Journals: Priority Journals; Cancer Journals

ENTRY MONTH: 19-806

ENTRY WEEK: 19-80603

AB . . . (PDGF) may be important for survival of FS cells. However, little is known about the interaction of cytokines with KSHV-infected **lymphocytes** from PEL. Therefore, we investigated what cytokines were produced by KSHV-infected PEL cell lines (KS-1, BC-1, BC-2), what cytokine receptors. . . antisense oligonucleotides had no effect on.

two

of B-cell lymphoma cell lines, which were not infected with KSHV. Addition
 IL-6 **antibody** did not inhibit clonal growth of any of the cell
 lines. Taken together, we have defined the cytokines and their receptors
 expressed on PEL cells and have found that these cells synthesized IL-6
 and **IL-6 receptors**; interruption of this
 pathway by IL-6 antisense oligonucleotides specifically prevented the
 growth of these cells. These findings will offer potential. . .
 CT Check Tags: **Human**; Support, Non-U.S. Gov't; Support, U.S. Gov't,
 P.H.N.
 Cell Division: DE, drug effects
 Cytokines: PD, pharmacology
 *Herpesvirus, Kaposi Sarcoma-Associated: IP, isolation. . .

L4 ANSWER 7 OF 15 MEDLINE DUPLICATE 3
 ACCESSION NUMBER: 1498447561 MEDLINE
 DOCUMENT NUMBER: 98427561
 TITLE: IL-6 functions in cynomolgus monkeys blocked by a
humanized antibody to human IL-6
 receptor.
 AUTHOR: Imaeki I; Saito H; Hasegawa M; Shinkura H; Kishimoto T;
 Ohsuga Y
 CORPORATE SOURCE: Fujii-Hitemba Research Laboratories, Chugai Pharmaceutical
 Co., Ltd, Tokyo, Japan.
 SOURCE: INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, 1999 Jul; 20
 (1):34-37.
 Journal code: GRI. ISSN: 0192-1501.
 PUB. COUNTRY: ENGLAND: United Kingdom
 Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 1999
 ENTRY WEEK: 1490341

TI IL-6 functions in cynomolgus monkeys blocked by a **humanized**
 antibody to **human IL-6** receptor.
 AB A **humanized antibody to the human**
 interleukin-6 receptor (IL-6R), hPM-1, blocked the interleukin-6 (IL-6)
 functions in normal cynomolgus monkey **lymphocytes** in vitro. The
 binding activity of hPM-1 to non-human primate IL-6R was
 examined in peripheral blood **lymphocytes** by flow cytometry. PM-1
 recognized the IL-6R on T **lymphocytes** of cynomolgus and rhesus
 monkeys, but did not on those of marmosets. The homology between
human IL-6R and its cynomolgus monkey counterpart was 97.3% in the
 extracellular domain of the amino acid sequence, as determined by. . .
 blood mononuclear cells. PM-1 inhibited two functional parameters in
 vitro
 in cynomolgus monkeys: (1), T-cell proliferation stimulated by
 phytohemagglutinin and **human IL-6**; (2), Immunoglobulin
 G-production evoked by Staphylococcus aureus Cowan-1- and **human**
 IL-6-stimulated B **lymphocytes**. These data show that hPM-1 binds
 to and functionally blocks the cynomolgus monkey **IL-6**
receptors.

CT Check Tags: Animal; Comparative Study; **Human**
 Amino Acid Sequence
 Antibodies, Monoclonal: IM, immunology
 *Antibodies, Monoclonal: PD, pharmacology
 Base Sequence
 Cell Lines
 Cells, Cultured
 Cross Reactions
 Tag: BI, . . .

L4 ANSWER 8 OF 16 MEDLINE DUPLICATE 4
 ACCESSION NUMBER: 1998368076 MEDLINE
 DOCUMENT NUMBER: 98368076
 TITLE: T-cell interleukin-6 receptor binding in patients with

myasthenia gravis.
 AUTHOR: Bingioanni P; Ricciardi R; Romano M R; Murri L; Muratorio A
 CORPORATE SOURCE: Department of Neurosciences, University of Pisa, Italy.
 SOURCE: JOURNAL OF THE NEUROLOGICAL SCIENCES, (1998 Jun 30) 158
 215-220.
 Journal code: JBJ. ISSN: 0022-510X.
 PUB. COUNTRY: Netherlands
 Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199801
 ENTRY WEEK: 1998104

AB Myasthenia gravis (MG) is a T-cell-dependent and **antibody**-mediated autoimmune disease of the neuromuscular junction, in which the cytokine network may be deranged. Specific receptors for interleukin (IL)-6, a cytokine with several effects on the neuroimmune system, have been found on **human lymphocytes**. The aim of the present study has been to assay IL-6 binding on peripheral blood T cells from MG patients. We found that T cells from MG patients have significantly more **IL-6 receptors** than those from controls (Bmax: 334 +/- 6 vs 251 +/- 4 (mean +/- SEM) receptors/cell). Such IL-6 binding sites. . . (mean +/- SEM) pM). The enhanced T-cell interleukin-6 binding is due to an increased number of interleukin-6 receptors on T-helper **lymphocytes**. These results are discussed in terms of MG immunopathogenesis, since it has been reported that activated T cells have increased amounts of **IL-6 receptors**.

CT Check Tags: Female; Human: Male
 Adult
 Aged
 Blood Cells: ME, metabolism
 Lymphocyte Transformation: PH, physiology
 Middle Age
 *Myasthenia Gravis: BL, blood
 Myasthenia Gravis: PA, . . .

L4 ANSWER 3 OF 16 UNSPATEFULL

ACCESSION NUMBER: 87851354 UNSPATEFULL
 TITLE: Diagnosis and treatment of cell proliferative disease having clonal macrophage involvement
 INVENTOR(S): McGrath, Michael J., Burlingame, CA, United States
 Herndler, Brian, San Francisco, CA, United States
 Sharamizu, Bruce, Pacifica, CA, United States
 PATENT ASSIGNEE(S): The Regents of the University of California, Oakland, CA, United States (U.S. corporation)

| | NUMBER | DATE |
|-----------------------|--|--------------|
| PATENT INFORMATION: | US 5639600 | 19970617 |
| APPLICATION INFO.: | US 1995-473040 | 19950606 (8) |
| RELATED APPLN. INFO.: | Continuation-in-part of Ser. No. US 1994-286745, filed in 5 Aug 1994 | |
| DOCUMENT TYPE: | Utility | |
| PRIMARY EXAMINER: | Bisson, Bradley L. | |
| LEGAL REPRESENTATIVE: | Boricovic, Earl Fish & Richardson P.C. | |
| NUMBER OF CLAIMS: | 11 | |
| EXEMPLARY CLAIM: | 1 | |
| NUMBER OF DRAWINGS: | 3 Drawing Figure(s); 2 Drawing Page(s) | |
| LINE COUNT: | 1717 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM The field of the invention relates to therapy for cell proliferative diseases; **human** immunodeficiency virus; a recombinant macrophage; methods of diagnosis of macrophage involvement in cell proliferative disease; kits for use in diagnosis; . . .

SUMM . . . the diseased tissue. Second, the macrophage is substantially eliminated from the diseased tissue by administering to the mammal (preferably a **human**) harboring the diseased tissue, a therapeutic agent that is in a formulation for preferential uptake by a macrophage. The administering. . .

SUMM . . . germ inhibitor, and gelonin (Mucuna) (Lifson, J. D., et al., supra). Trichosanthin and momorcharin inhibit expression of HIV antigens in **human** blood cells including macrophages (Lifson, J. D., et al., supra).

SUMM . . . targeting moiety can be linked to a drug either directly or indirectly by carrier molecules such as serum albumin (particularly **human** serum albumin), polyaminoacids, dextran, and the like, by methods well known to those skilled in the art. The use of. . .

SUMM . . . means an oncogene which increases the probability of the development of neoplasms (particularly malignant tumors) in a mammal (particularly a **human**). A gene associated with cell proliferation also includes a cell growth suppressing gene such that decreased gene expression of a. . .

SUMM By "HIV" is meant a **human** immunodeficiency virus of strains HIV-1, HIV-2, or other variants.

SUMM . . . of the invention are preferably designed for the diagnosis and treatment of clonal HIV- and non-HIV-associated macrophage-induced cancer in a **human**.

DRWD FIG. 2 shows a schematic diagram of HIV insertion into **human** c-sis.

DRWD FIG. 3 is a portion of the **human** c-sis proto-oncogene sequence into which HIV has inserted at intron 1. The sequenced DNA was IPCK products from macrophages obtained. . .

DETD . . . and hematopoiesis (Aizawa, M. et al., Immunol Review (1992) 127:5-6). Many cell types, including monocyte/macrophages, fibroblasts, endothelia, B and T **lymphocytes**, chondrocytes, astrocytes and osteinocytes are capable of producing IL-6. IL-6 can exert growth-inducing, growth-inhibitory or differentiation inducing activities depending upon. . . cells. In regard to lymphocytic stimulation IL-6 has been shown to be involved in 1) terminal differentiation of B-cells into **antibody** producing plasma cells; 2) induction of IL-2 and IL-3 receptors and differentiation of T-cells; and 3) IL-6 has been shown. . . of myeloma and hybridoma cells (Woodruff, C., et al., DNA and Cell Biology (1992) 11:587-592). IL-6 may cause transformation of **IL-6 receptor** expressing cells (Takahara, M., et al., J Exp Med 1990) 171:389. IL-6 producing macrophages and endothelial cells were shown to. . .

DETD . . . invention involves probing the restriction digested and gel separated DNA with nucleic acid probes that hybridize to specific mammalian (preferably, **human**) genomic DNA regions.

DETD SCID mice are injected with **human** splenic tissue containing clonal HIV-integrated macrophages (e.g., tissue from Case 10). Control SCID mice are injected with normal (no HIV). . .

DETD . . . derived growth factor B gene (PDGF-B) as shown in FIG. 3. A viral ITR sequence is shown inserted in the **human** c-sis gene (PDGF-B gene).

DETD . . . in experimental fat-fed rabbit systems (Rosenfeld, M. E. and Ross, R. (1990) Arteriosclerosis 10:680-687) and in cell cycle analysis of **human** plaques (Gordon, D. et al. (1990) P.N.A.S. U.S.A. 87:4600-4604), it is clear that in situ macrophage proliferation is comparable in. . .

DETD In **human** atherosclerotic lesions, PDGF-A and PDGF-B mRNA and protein are expressed in endothelial cells, smooth muscle cells, and macrophages (Parrett, T. . .

DETD . . . from macrophages of the atherosclerotic plaque tissue. Using the v-cis probe (Oncor, Gathersberg, Md.) which hybridizes to sequences in the **human** PDGF-B gene, it was found that the PDGF-B gene was rearranged. Thus, the HIV insertion indicated by IPCK is shown. . .

CLM What is claimed is:

- . . . in a sample, wherein said method comprises: determining by a nucleic acid hybridization technique the presence in macrophage DNA of **human immunodeficiency virus (HIV)** integration at a location relative to a cell proliferative oncogene wherein said location is further characterizes in. . .

L4 ANSWER 10 OF 16 BIOSIS COPYRIGHT 2000 BIOSIS

ACCESSION NUMBER: 1997:411491 BIOSIS

DOCUMENT NUMBER: PREV19970702424

TITLE: Two-color flow cytometric analysis of cytokine receptors and surface markers on blood cells.

AUTHOR(S): Maruyama, Soichi (1); Aoki, Sadao; Tsukada, Nobuhiro; Nomoto, Nobuhiko; Aizawa, Yoshifusa; Takahashi, Hoya

CORPORATE SOURCE: (1) First Dep. Internal Med., Niigata Univ. Sch. Med., Asahi-machi 5-1-757, Niigata 951 Japan

SOURCE: Acta Medica et Biologica, 1997) Vol. 45, No. 2, pp. 39-44.

ISSN: 0304-3814.

DOCUMENT TYPE: Article

LANGUAGE: English

AB. . . a specified cell population, two-color flow cytometric analysis of cytokine receptors and surface markers using fluorescence labeled cytokines and monoclonal **antibodies** was performed. In normal peripheral blood cells, granulocytes expressed granulocyte colony-stimulating factor (G-CSF) receptor and interleukin-6 (**IL-6 receptor**), but mostly expressed interleukin-3 (IL-3) receptor weakly. Monocytes were positive for each receptor. In **lymphocytes**, CD3 positive T cells did not express any of these receptors; however, CD19 positive B cells expressed G-CSF receptor, IL-3 receptor, and partly expressed **IL-6 receptor**. In clinical cases, leucemic cells of acute myeloid leukemia (AML) patients tended to show the same characteristics as normal granulocytes.

15 Major Concepts

Biochemistry and Molecular Biophysics: Blood and Lymphatics (Transport and Circulation); Cell Biology; Clinical Immunology (**Human** Medicine, Medical Sciences); Endocrine System (Chemical Coordination and Homeostasis); Hematology (**Human** Medicine, Medical Sciences); Membranes (Cell Biology); Oncology (**Human** Medicine, Medical Sciences)

OEGN Super Taxa

Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

OEGN Organism Name

human (Hominidae)

OEGN Organism Superterms

animals; chordates; **humans**; mammals; primates; vertebrates

L4 ANSWER 11 OF 16 USPATFEE

ACCESSION NUMBER: 96:111306 USPATFULL

TITLE: Diagnosis of cancer having clonal macrophage involvement

INVENTOR(S): McGrath, Michael S., Burlingame, CA, United States
Kornblum, Brian, San Francisco, CA, United States
Shirahata, Bruce, Pacifica, CA, United States

PATENT ASSIGNEE(S): The Regents of the University of California, Oakland, CA, United States (U.S. corporation)

| | NUMBER | DATE |
|-----------------------|--------------------|--------------|
| PATENT INFORMATION: | US 5,807,111 | 19961203 |
| APPLICATION INFO.: | US 1994-266749 | 19940805 (8) |
| DOCUMENT TYPE: | Utility | |
| PRIMARY EXAMINER: | Conez, W. Gary | |
| ASSISTANT EXAMINER: | Sisson, Bradley L. | |
| LEGAL REPRESENTATIVE: | Bozicevic, Karl | |

NUMBER OF CLAIMS: 13
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT: 1207

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM The field of the invention relates to cancer therapy; **human** immunodeficiency virus; a recombinant macrophage; methods of diagnosis of macrophage involvement in cancer development; kits for use in diagnosis; and.

SUMM . . . in the cancer. Second, the macrophage is substantially eliminated from the cancerous tissue by administering to the mammal (preferably a **human**) harboring the cancerous tissue, a therapeutic agent that is in a formulation for preferential uptake by a macrophage. The administering. . .

SUMM . . . germ inhibitor, and gelonin (Kuefun) (Lifson, J. D., et al., supra). Phorbolanthra and momorcharin inhibit expression of HIV antigens

in **human** blood cells including macrophages (Lifson, J. D., et al., supra).

SUMM . . . targeting moiety can be linked to a drug either directly or indirectly by carrier molecules such as serum albumin (particularly **human** serum albumin), polyaminocarboxylic acids, dextran, and the like, by methods well known to those skilled in the art. The use of. . .

SUMM . . . means an oncogene which increases the probability of the development of neoplasm (particularly malignant tumors) in a mammal (particularly a **human**). A gene associated with cell proliferation also includes a cell growth suppressing gene such that decreased gene expression of. . .

SUMM B; "HIV" is meant a **human** immunodeficiency virus or strains HIV-1, HIV-2, or other variants.

SUMM . . . of the invention are preferably designed for the diagnosis and treatment of clonal HIV- and non-HIV-associated macrophage-induced cancer in a **human**.

DETD . . . and hematopoiesis (Aizawa, S. et al., Immunol Review (1992) 127:35-50). Many cell types, including monocyte/macrophages, fibroblasts, endothelia, B and T **lymphocytes**, chondrocytes, astrocytes and mastocytes are capable of producing IL-6. IL-6 can exert growth-inducing, growth-inhibitory or differentiation inducing activities depending upon. . . cell. In regard to lymphocytic stimulation IL-6 has been shown to be involved in 1) terminal differentiation of B-cells into **antibody** producing plasma cells; 2) induction of IL-2 and IL-2 receptors and differentiation of T-cells; and 3) IL-6 has been shown. . . of myeloma and hybridoma cells (Woodruff, C., et al., DNA and Cell Biology (1992) 11:587-592). IL-6 may cause transformation of IL-6

receptor expressing cells (Tohyama, N., et al., J Exp Med (1990) 171:383). IL-6 producing macrophages and endothelial cells were shown to. . .

DETD . . . invention involves probing the restriction digested and gel separated DNA with nucleic acid probes that hybridize to specific mammalian (preferably, **human**) genomic DNA regions.

DETD SCID mice are injected with **human** splenic tissue containing clonal HIV-integrated macrophages (e.g., tissue from Case 10). Control SCID mice are injected with normal (no HIV). . .

CLM What is claimed is:

. . . macrophages from other cells of said sample; c) isolating DNA from said macrophages; and d) determining the presence of a **human** immunodeficiency virus (HIV) integrated into the fur gene.

5. The method of claim 1 wherein said **human** immunodeficiency virus is integrated into the z exon of the fur gene.

6. The method of claim 1 wherein said mammal is a **human**.

ACCESSION NUMBER: 93229747 MEDLINE
DOCUMENT NUMBER: 93229747
TITLE: Interleukin-6 inhibits the proliferation of B-chronic lymphocytic leukemia cells that is induced by tumor necrosis factor-alpha or -beta.
AUTHOR: Auerka D; Mahr J; Novick D; Engelmann H; Kahn Y; Levo Y; Wallach D; Rorel M
CORPORATE SOURCE: Department of Molecular Genetics and Virology, Weizmann Institute of Science, Rehovot, Israel.
SOURCE: BLOOD, 1993 Apr 15; 81 (3): 2076-84.
Jurnal code: A43. ISSN: 0006-4971.
PUB. COUNTRY: United States
Jurnal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals
ENTRY MONTH: 199317

AB Tumor necrosis factor (TNF)-alpha acts as a growth stimulatory factor on leukemic B **lymphocytes** from many patients with chronic lymphocytic leukemia (CLL). Because TNF induces production of interleukin-6 (IL-6), which has been shown to . . . TNF on B-CLL cells. In fact, we found that IL-6 is an inhibitor of B-CLL growth. The addition of recombinant **human** IL-6 markedly decreased the TNF-induced B-CLL growth, and this decrease was even greater when soluble **IL-6 receptor**, known to act as IL-6 agonist, was added with recombinant IL-6. Conversely, neutralizing monoclonal **antibodies** to IL-6 and to the **IL-6 receptor** potentiated the growth stimulation of TNF on B-CLL cells, in line with the possibility that IL-6 functions as a negative. . .

CT Check Tags: Animal: **Human**; Support, Non-U.S. Gov't

B-lymphocytes: ME, metabolism
B-lymphocytes: PA, pathology
Cell Division
Cell Transformation, Viral
CrO Cells: ME, metabolism
Escherichia coli: ME, metabolism
Fensters
Herpesvirus 4, Human
Interleukin-6: ME, metabolism
*Interleukin-6: PA, pharmacology
Leukemia, B-Cell, Chronic: BL, blood
*Leukemia, B-Cell, Chronic: PA, pathology
*Lyphotexin: . . .

L4 ANSWER 13 OF 16 MEDLINE

DUPLICATE 6

ACCESSION NUMBER: 93063804 MEDLINE
DOCUMENT NUMBER: 93063804
TITLE: Effect of cell-derived growth factors and cytokines on the clonal outgrowth of EBV-infected B cells and established lymphoblastoid cell lines.
AUTHOR: Iversen P; Chang X M; Chlun M; Zeuthen J; Borrebaeck C A
CORPORATE SOURCE: Department of Immunotechnology, Lund University, Sweden.
SOURCE: HUMAN ANTIBODIES AND HYBRIDOMAS, (1993 Jul) 4 (3): 115-23.
Jurnal code: A7A. ISSN: 0956-960X.
PUB. COUNTRY: United States
Jurnal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199317

AB Epstein-Barr virus (EBV) is a potent inducer of polyclonal B **lymphocyte** proliferation and is widely used as a tool for the establishment of B cell lines producing **human** monoclonal **antibodies**. However, because of low transformability, low clonability, and the inherent instability of EBV-infected B cells, valuable **antibody**-producing B cells are often lost during this

procedure. We have here examined various cell-derived cytokines for their ability to enhance. . . and monocyte cell lines were less capable than peripheral blood mononuclear cells in enhancing cellular outgrowth and cloning. Furthermore, the **human** T cell hybridoma cell line MP6 that secretes a B cell growth and differentiation factor, recently identified as an **interferon**. . . level. The present results also suggest that one potential role of the MP6-derived thioredoxin could be the up regulation of **IL-6 receptor** expression in EBV-infected B cells.

CT Check Tags: **Human**; Support, Non-U.S. Gov't
 B-Lymphocytes: DL, drug effects
 B-Lymphocytes: MI, microbiology
 *B-Lymphocytes: PH, physiology
 Cell Line
 Cell Line, Transformed
 *Cell Transformation, Viral
 *Cytokines: PD, pharmacology
 DNA: BI, biosynthesis
 *Growth Substances: PD, pharmacology
 *Herpesvirus 4, Human: GE, genetics
 *Lymphocyte Transformation: DE, drug effects
 Receptors, Immunologic: AN, analysis
 Thioredoxin: PD, pharmacology

L4 ANSWER 14 OF 16 MEDLINE DPLICATE 7
 ACCESSION NUMBER: 9 40184 MEDLINE
 DOCUMENT NUMBER: 9 40184
 TITLE: Expression of interleukin-6 receptor on blood lymphocytes without in vitro activation.
 AUTHOR: Lutz E; Flege L
 CORPORATE SOURCE: Department of Clinical Immunology, Flinders Medical Centre,
 South Australia.
 SOURCE: IMMUNOLOGY, (1992 Jun) 76 (2) 338-40.
 Journal code: GH. ISSN: 0019-2805.
 PUB. COUNTRY: ENGLAND; United Kingdom
 Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals; Cancer Journals
 ENTRY MONTH: 1992

AB A monoclonal **antibody** against the interleukin-6 receptor (IL-6R) has been used in a high-sensitivity immunofluorescence technique to study receptor expression in unstimulated blood **lymphocytes**. Most CD4 cells express **IL-6 receptor**, whilst a small and variable proportion of CD8 and B cells are positive. CD4+ cells express higher levels of receptor. . .

CT Check Tags: **Human**
 B-Lymphocytes: MI, immunology
 CD4-positive T-Lymphocytes: MI, immunology
 *Lymphocytes: MI, immunology
 *Receptors, Immunologic: AN, analysis
 T-Lymphocytes: MI, immunology

L4 ANSWER 15 OF 16 MEDLINE DPLICATE 8
 ACCESSION NUMBER: 9233185 MEDLINE
 DOCUMENT NUMBER: 9233185
 TITLE: IL-6 enhances the generation of cytolytic T lymphocytes in the allogeneic mixed leucocyte reaction.
 AUTHOR: Ming J H; Steinman R M; Granelli-Piperno A
 CORPORATE SOURCE: Laboratory of Cellular Physiology and Immunology, Rockefeller University, New York, NY 10021.
 CONTRACT NUMBER: A114775 (NIAID)
 5-T32-GN07739 (NIGMS)
 SOURCE: CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (1992 Jul) 89 (1) 148-53.
 Journal code: LD7. ISSN: 0009-9104.

PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199210

AB Cytolytic T **lymphocytes** (CTL) require soluble proteins termed lymphokines to develop lytic activity. In this report we have studied two of the lymphokines. . . . leucocyte reaction (MLR). High doses of dendritic cells induced lytic activity from purified CD8+ cells in both the murine and **human** MLR. Under these conditions, IL-2 and IL-6 were endogenously produced and secreted. **Antibodies** to IL-2 or the IL-2 receptor blocked CTL formation; however, anti-IL-6 **receptor antibodies** only partially inhibited the response while anti-IL-6 **antibodies** were largely ineffective. When limiting numbers of antigen-presenting cells were used CTL failed to develop, and neither IL-2 nor IL-6. . . .
CT Check Tags: Animal; **Human**; Support, U.S. Gov't, P.H.S.
Antibodies: TM, immunology
Cells, Cultured
Cytotoxicity, Immunologic
Dendritic Cells: TM, immunology
Dendritic Cells: NL, metabolism
Dose-response. . . .

L4 ANSWER 16 OF 16 MEDLINE

ACCESSION NUMBER: 9435423 MEDLINE

DOCUMENT NUMBER: 9435423

TITLE: Production and secretion of BSF2/IL6 in a case of hairy cell leukemia with polyclonal hypergammaglobulinemia.

AUTHOR: Shiohara M; Kawanishi Y; Nakano M; Ohdo T; Toyama K

CORPORATE SOURCE: First Department of Internal Medicine, Tokyo Medical College.

SOURCE: NIPPON KETSUKEI GAKKAI ZASSHI. ACTA HAEMATOLOGICA JAPONICA,

(1991 May) 53: 3: 182-8.

Journal code: JSTL ISSN: 0001-5806.

PUB. COUNTRY: Japan.

Journal; Article; JOURNAL ARTICLE

LANGUAGE: Japanese

ENTRY MONTH: 199111

AB 8716 mg/dL. To elucidate the mechanism of the PHG, we investigated whether hairy cells produce interleukin 6 (IL-6) and express **IL-6 receptor**. The culture supernatant of these hairy cells increased 3H-thymidine uptake of a IL-6 dependent hybridoma clone (HBH) in a dose-dependent manner. These cells were stained with anti-IL-6 **antibody** using immuno-cytochemical technique. Our results suggested that these hairy cells produce and secrete IL-6. Immunocytochemical staining with anti **IL-6 receptor antibody** and the binding assay with 125I-labelled recombinant IL-6 revealed that these cells express little

or

no receptors for IL-6. It. . . . an autocrine growth factor for these cells but may play a role in development of PHG by stimulating normal B **lymphocytes** to produce an excessive amount of immunoglobulin.

CT Check Tags: Case Report; Female; **Human**; Support, Non-U.S. Gov't

B-Lymphocytes: TM, immunology

English Abstract

*Hypergammaglobulinemia: ET, etiology

*IgG

Interleukin-6: AN, analysis

*Interleukin-6: BL, biosynthesis

Interleukin-6: SE,

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L1 136 (IL-6 (S) RECEPTOR AND ANTIBODY AND LYMPHOCYTE AND TREATMENT

=> s (il-6 (s) receptor) (s) antibody (p) lymphocyte (p) treatment

L1 139 (IL-6 (S) RECEPTOR (S) ANTIBODY (P) LYMPHOCYTE (P) TREATMENT

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PROCESSING COMPLETED FOR L3

L3 21 DUP REM 13 (38 DUPLICATES REMOVED)

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|-------------------|---|---------|-------------|
| L4 | ANSWER 1 OF 21 | MEDLINE | DUPLICATE 1 |
| ACCESSION NUMBER: | 20 0094687 | MEDLINE | |
| DOCUMENT NUMBER: | 20 094687 | | |
| TITLE: | Expression of functional interleukin-15 receptor and autocrine production of interleukin-15 as mechanisms of tumor propagation in multiple myeloma. | | |
| AUTHOR: | Tinkhofer I; Marachitz I; Herr T; Egle A; Greil R | | |
| CORPORATE SOURCE: | Laboratory of Molecular Cytology, Department of Internal Medicine, University of Innsbruck, Innsbruck, Austria. | | |
| SOURCE: | BLOOD, (2000 Jan 15) 95 (2) 610-8. | | |
| | Journal code: ABG. ISSN: 0006-4971. | | |
| PUB. COUNTRY: | United States | | |
| | Journal: Article; (JOURNAL ARTICLE) | | |
| LANGUAGE: | English | | |
| FILE SEGMENT: | Abridged Index Medicus Journals; Priority Journals; Cancer Journals | | |
| ENTRY MONTH: | 200004 | | |

ENTRY WEEK: 20000401

AB Interleukin-15 (IL-15) induces proliferation and promotes cell survival of

human T And B **lymphocytes**, natural killer cells, and neutrophils. Here we report the constitutive expression of a functional IL-15 **receptor** (IL-15R) in 6 of 6 myeloma cell lines and in CD38(high)/CD45(low) plasma cells belonging to 14 of 14 patients with. . . the rate of spontaneous apoptosis, and the degree of this effect was comparable to the pro-apoptotic effect of depleting autocrine IL-6 by **antibody** targeting. IL-15 was also capable of substituting for autocrine IL-6 in order to promote cell survival and vice versa. In short-term cultures of primary myeloma cells, the addition of IL-15. . . reduced the percentage of tumor cells

spontaneously undergoing apoptosis. Furthermore, IL-15 lowered the responsiveness to Fas-induced apoptosis and to cytotoxic **treatment** with vincristine and doxorubicin but not with dexamethasone. These data add IL-15 to the list of important factors promoting survival. . .

L4 ANSWER 2 OF 21 MEDLINE

DUPLICATE 2

ACCESSION NUMBER: 20002300 MEDLINE

DOCUMENT NUMBER: 20000000

TITLE: The engineered human anti-tumor necrosis factor-alpha antibody CDP571 inhibits inflammatory pathways but not T cell activation in patients with rheumatoid arthritis.
AUTHOR: Day E H; Rankin E C; Kassam S D; Vetterlein O; Garyfallos A; Partridge C T; Sowth H; Eastell R; Kingsley G H; Tengblad A; Panayi G S

CORPORATE SOURCE: Department of Clinical and Molecular Rheumatology, The Royal Hospital Medical and Dental School, London, United Kingdom.

SOURCE: JOURNAL OF RHEUMATOLOGY, 1999 Nov; 26 (11): 2310-7.
Journal Code: JWX. ISSN: 0369-162X.

PUB. COUNTRY: Canada

CLINICAL TRIAL

CONTROLLED CLINICAL TRIAL

Journal: Article; JOURNAL ARTICLE

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 2000

ENTRY WEEK: 20000401

AB **OBJECTIVE:** We investigated the effect of an engineered human anti-tumor necrosis factor-alpha **antibody**, CDP571, on immune functions as well as bone and cartilage turnover in patients with rheumatoid arthritis (RA) in a placebo controlled trial. We also assessed the effects of repeated **treatment** with CDP571 in an open label continuation study. **METHOD:** Thirty-six patients were treated with either placebo or 1, 1, or 10 mg/kg of CDP571 given as an intravenous infusion. The followup period was 4 weeks. **Lymphocyte** phenotype, soluble CD4 (sCD4), soluble interleukin 2 **receptor** (sIL-2R), IL-6, and stromelysin levels in the blood were measured before and after **treatment**; bone and cartilage markers (pyridinoline, deoxypyridinoline, N-terminal telopeptide) were similarly assessed in the urine. Patients who completed a placebo controlled trial of CDP571 were offered further **treatment** with CDP571. They received a maximum of 2 further doses of 1 mg/kg (7 patients) or 10 mg/kg (9 patients) in an open study. **RESULTS:** Plasma IL-6 level was statistically significantly reduced in the 1 and 10 mg/kg groups. In the 10 mg/kg group, there were also. . . levels. Repeat doses of CDP571 were well tolerated and continued to suppress the acute phase response

and

disease activity. **CONCLUSION:** **Treatment** with 10 mg/kg of CDP571 reduced IL-6 and surrogate markers of bone turnover in RA, suggesting that CDP571 might prevent joint damage in RA. Since there was no effect on **lymphocyte** markers despite the marked reduction in inflammation, CDP571 appears to have no effect on ongoing CD4 T cell

activation.

L4 ANSWER 3 OF 21 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 000004265 MEDLINE
DOCUMENT NUMBER: 011265
TITLE: Long-term follow-up of the changes in circulating
cytokines, soluble cytokine receptors, and white blood
cell
subset counts in patients with rheumatoid arthritis (RA)
after monoclonal anti-TNF alpha antibody therapy.
AUTHOR: Nakama S; Saeki Y; Hima T; Sasai M; Nishioka K; Ishida H;
Mizukawa M; Saemura M; McCloskey R; Kishimoto T
CORPORATE SOURCE: Department of Molecular Medicine, Osaka University Medical
School, Suita City, Japan.
SOURCE: JOURNAL OF CLINICAL IMMUNOLOGY, (1999 Sep) 19 (5) 305-13.

Journal Code: JEC. ISSN: 0271-9142.
PUB. COUNTRY: United States
JOURNAL TITLE: JOURNAL OF CLINICAL IMMUNOLOGY
JOURNAL; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Library Journals
ENTRY MONTH: 1999
ENTRY WEEK: 1999104

AB To investigate the mechanism of the long-lasting efficacy of chimeric
monoclonal anti-TNFalpha **antibody** (A2) therapy for rheumatoid
arthritis (RA), eight patients with refractory RA were treated with a
single infusion of cA2 and the change in circulating cytokines (IL-1,
IL-6, TNFalpha, and IL-10), soluble cytokine
receptors (TNF-R1, RII, and sIL-6R) and peripheral white blood
cell (WBC) subset counts were followed up long-term (12 weeks) after cA2.
... All patients, as reported elsewhere. Moreover, five of the eight
patients showed prolonged clinical responses (>12 weeks). The elevated
serum IL-6 and TNF-R1 (or RII) levels before
treatment rapidly decreased after **treatment**. The serum
IL-10 levels also significantly elevated before **treatment**. The
elevations of serum IL-10 levels were augmented after **treatment**
and stayed higher than the baseline in four patients with prolonged
clinical responses. No significant TNFalpha, IL-1alpha and -beta, or
sIL-6R were detected in the sera of the patients before **treatment**
and during the whole study period. On the other hand, peripheral
lymphocytes as well as total WBC and neutrophils increased for 4
weeks after **treatment**. However, thereafter, only the
lymphocyte count decreased gradually and stayed below the baseline
long-term (12 weeks). FAIS analysis revealed the predominance of T
lymphocytes in the decrease in **lymphocyte** counts. These
results suggest that the augmentation of IL-10 production and the
decrease
in T cells might partly contribute to the long-lasting efficacy of cA2
treatment in RA.

L4 ANSWER 4 OF 21 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 199914127 MEDLINE
DOCUMENT NUMBER: 9144127
TITLE: Cytokines in inflammatory bowel disease.
AUTHOR: Figler G; Andus T
CORPORATE SOURCE: Department of Internal Medicine I, University of
Hamburg, Germany.
SOURCE: WILEY JOURNAL OF SURVEY, (1998 Apr) 22 (4) 382-9. Ref:
16
Journal Code: XCB. ISSN: 0364-2313.
PUB. COUNTRY: United States
JOURNAL; Article; JOURNAL ARTICLE
General Review; (REVIEW)
REVIEW, ACADEMIC
LANGUAGE: English

ENTRY MONTH: 199706
ENTRY WEEK: 1997604

AB Cytokines play a central role in the modulation of the intestinal immune system. They are produced by **lymphocytes** (especially T cells of the Th1 and Th2 phenotypes), monocytes, intestinal macrophages, granulocytes, epithelial cells, endothelial cells, and fibroblasts. They have proinflammatory functions [interleukin-1 (IL-1), tumor necrosis factor (TNF), IL-6, IL-8, IL-1.] or antiinflammatory functions [interleukin-1 **receptor** antagonist (IL-1ra), IL-4, IL-10, IL-11, transforming growth factor beta (TGF beta)]. Mucosal and systemic concentrations of many pro- and antiinflammatory . . . acid (TNBS) model, or the genetically engineered model of IL-10 knockout mice. Based on these findings a rationale for cytokine **treatment** was defined. The first clinical trials using neutralizing monoclonal **antibodies** against TNF alpha (CA2) or the antiinflammatory cytokine IL-10 have shown promising results. However, many questions must be answered before. . .

L4 ANSWER 5 OF 21 MEDLINE
ACCESSION NUMBER: 9731930J MEDLINE
DOCUMENT NUMBER: 9731930J
TITLE: Decreased expression of ICAM-1 and its induction by tumor necrosis factor on breast-cancer cells in vitro.
AUTHOR: Erdinsky A C; Brodowicz T; Wilttschke C; Czerwenka K; Michl I; Krainer M; Zielinski C C
CORPORATE SOURCE: Department of Internal Medicine I, University Hospital, Vienna, Austria.
SOURCE: INTERNATIONAL JOURNAL OF CANCER, 1997 Jun 11; 71: 61086-90.
JOURNAL CODE: GQU. ISSN: 0010-7136.
PUB. COUNTRY: United States
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199706
ENTRY WEEK: 1997604

AB . . . lower than that of benign breast cells or normal breast epithelium. Of various cytokines tested, including recombinant human (rh) interleukin-6 (IL-6), rh tumor necrosis factor alpha (TNF-alpha), interleukin-1 (IL-1), granulocyte/macrophage-colony-stimulating-factor (GM-CSF), interferon-alpha (IFN-alpha) and interferon-gamma (IFN-gamma), only TNF was able. . . unstimulated or lymphokine-stimulated killer (LAK) cells to recognize and lyse native or TNF-stimulated breast-cancer cells was studied. Whereas neither unstimulated **lymphocytes** or LAK cells were able to lyse untreated breast-cancer cells deficient for ICAM-1 expression, pre-**treatment** of tumor cells with TNF led to increased tumor-cell lysis. Anti-ICAM-1 **antibodies**, and pre-**treatment** of tumor cells with anti-TNF-**receptor antibodies**, abrogated these findings, corroborating their specificity. We thus conclude that the defective expression of ICAM-1 in our model might constitute. . .

L4 ANSWER 5 OF 21 MEDLINE
ACCESSION NUMBER: 9741935J MEDLINE
DOCUMENT NUMBER: 9741935J
TITLE: Medroxyprogesterone acetate reduces the in vitro production of cytokines and serotonin involved in anorexia/cachexia and emesis by peripheral blood mononuclear cells of cancer patients.
AUTHOR: Mantovani G; Macciolo A; Esu S; Lai P; Santona M C; Massa E;
Plessi D; Melis G B; Del Giudice G S
CORPORATE SOURCE: Department of Medical Oncology, University of Cagliari, Italy.

SOURCE: EUROPEAN JOURNAL OF CANCER, (1997 Apr) 33 (4) 602-7.
Journal code: ARV. ISSN: 0959-8049.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal: Article: (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199711
ENTRY WEEK: 19971101

AB Medroxyprogesterone acetate (MPA) is widely used in oncology both in the **treatment** of hormone-related cancers and as supportive therapy in anorexia/cachexia syndrome (ACS), but conclusive data are not yet available to explain. . . . It characterised by weight loss, changes in metabolism, reduction of appetite, nausea and vomiting. Several cytokines,

mainly interleukin (IL)-1, IL-2, IL-6 and tumor necrosis factor alpha (TNF alpha), are involved in the pathogenesis of ACS. Additionally, nausea and vomiting can be mediated by factors

including serotonin (5-HT) production and/or release by preneoplastic cells including activated T **lymphocytes**. In the present study, we report the effect of MPA on peripheral blood mononuclear cells (PBMC) from 10 cancer patients. . . . (5 male and 5 female, 3 colon, 1 lung and 1 ovary). The proliferative response of PBMC to PHA, anti-CD3 monoclonal **antibody** (MAB) or recombinant IL-2 (rIL-2), the production of IL-1 beta, IL-2, IL-6, TNF alpha and 5-HT by PHA-stimulated PBMC and the expression of **lymphocyte** membrane-bound IL-2 **receptor** (IL-2R) subunits (CD25 and CD122) were studied. The addition of MPA significantly reduced the PBMC proliferative response to PHA and anti-CD3 MAB but not to rIL-2. MPA 0.2 microgram/ml was also capable of reducing the levels of IL-1 beta, IL-6, TNF alpha and 5-HT produced in culture by PHA-stimulated PBMC, whereas it did not induce any change in the percentage. . . .

L4 ANSWER 2 OF 11 MEDLINE

DUPLICATE 7

ACCESSION NUMBER: 97341241 MEDLINE

DOCUMENT NUMBER: 97341241

TITLE: A comparative study of the in vitro immunomodulatory activity of human intact immunoglobulin (7S IVIG), F(ab')2 fragments (5S IVIG) and Fc fragments. Evidence for post-transcriptional IL-2 modulation.

AUTHOR: Nettekauer G; Herold M; Eibl H; Glassl H; Schwaighofer H; Huber C; Pachter A; Fichtl M; Niederwieser D

CORPORATE SOURCE: Department of Internal Medicine, University Hospital, Innsbruck, Austria.

SOURCE: IMMUNOLOGY, (1997 Feb) 90 (2) 212-8.

Journal code: GHT. ISSN: 0019-2805.

PUB. COUNTRY: ENGLAND: United Kingdom

Journal: Article: (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 199702

ENTRY WEEK: 19970204

AB During the past few decades intravenous immunoglobulin (IVIG) has been used successfully in the **treatment** of various immunoregulatory disorders. **Treatment** results have been attributed to immunomodulation mainly via Fc **receptors** or by anti-idiotypic **antibodies** to disease-causing autoantibodies. From the present study it is clearly evident that 7S IVIG (intact immunoglobulin) as well as 5S . . . have a potent immunomodulatory capacity. We demonstrate

that mainly 7S IVIG inhibits alloantigen-induced T-cell proliferation and generation of cytotoxic T **lymphocytes**. Reduced interleukin-2 (IL-2) protein levels in culture supernatants of IVIG-supplemented mixed **lymphocyte** reactions (MLR) but unchanged IL-2 mRNA levels strongly argue in favour of a post-transcriptional interference of IVIG with cytokines and/or cytokine production. Interferon-gamma (IFN-gamma),

soluble IL-2 **receptor** (sIL-2P) and monokines such as IL-1 beta, **IL-6**, IFN-alpha and tumour necrosis factor (TNF-alpha) were not affected by IVIG supplementation to MLR. Fc fragments were superior to F(ab')₂-containing.

L4 ANSWER 8 OF 21 MEDLINE DUPLICATE 8
 ACCESSION NUMBER: 9227711 MEDLINE
 DOCUMENT NUMBER: 9227711
 TITLE: Functional analysis of an autoantigen reactive B cell clone

AUTHOR: Kobayashi K; Hara T; Kakishita E
 CORPORATE SOURCE: Second Department of Internal Medicine, Hyogo College of Medicine.

SOURCE: KYUJAKHI, (1994 Dec) 35 (5) 844-55.
 Journal code: JST. ISSN: 0300-9157.

PUB. COUNTRY: Japan
 Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: Japanese

ENTRY MONTH: 1997 6

ENTRY WEEK: 1997 614

AB . . . provides a good model for the study on the pathogenesis of systemic lupus erythematosus with massive involvement of abnormal T **lymphocytes** in the spleen and lymph nodes. However, a direct role of B cells of MRL/lpr mice in autoimmune responses is not. . . exhibit rosette formation against blood cells treated with bromelain (Br-RBC) at

a frequency of more than 90%, and to express DNA-**receptor** (DNA-R) on its surface by FACS analysis with biotin-labeled ssDNA. In contrast, the

parental 1.52 M did not form rosettes. . . membrane of 2.52 M was significantly lower compared with that of MRL27.4. Interestingly, MRL27.4 produced a high titer of IgM-anti-ssDNA **antibodies** and

IL-6 after treatment with the purified RBC membrane or immobilized RBC. On the other hand, the parental 2.52 M neither produce IgM-anti-ssDNA **antibodies** nor **IL-6** under the same conditions. The results suggest that MRL27.4 is an autoantigen reactive B cell clone derived from MRL/lpr mice. . .

and its surface DNA-R, by itself, function to autoantigens. In this process, there might be an autocrine network mediated by **IL-6**. In conclusion, MRL27.4 provides a good model for the study on the direct function of B cells of MRL/lpr mice. . .

L4 ANSWER 9 OF 21 MEDLINE DUPLICATE 9
 ACCESSION NUMBER: 9613704 MEDLINE
 DOCUMENT NUMBER: 9613704
 TITLE: IFN-alpha-mediated suppression of low-affinity Fc(epsilon) receptors on Peyer's patch lymphocytes and augmentation of soluble CD23: implications for IgE responses.

AUTHOR: Heller H; Bluth M H; Chico S M; Durkin H G; Audi D L
 CORPORATE SOURCE: Department of Pathology, State University of New York Health Science Center at Brooklyn, 11203, USA.

SOURCE: JOURNAL OF LEUKOCYTE BIOLOGY, (1996 May) 59 (5) 725-7.
 Journal code: JWB. ISSN: 0741-5400.

PUB. COUNTRY: United States
 Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Primary Journals; Cancer Journals

ENTRY MONTH: 1996 5

AB The ability of interleukin (IL)-6 or interferon-alpha (IFN-alpha) to regulate expression of low-affinity Fc(epsilon) **receptor** (CD23) and serum levels of CD23 was studied in benzylpenicilloyl-k-lysole lipet hemocyanin-sensitized BALB/c mice at the peak of a hapten-specific immunoglobulin E (IgE) **antibody**-forming cell (AFC) response. These responses are analogous to those

observed in human atopic disease. To induce peak IgE responses, mice. . . micrograms) in aluminum hydroxide gel (alum) on days 0, 21, and 42. On day 44, mice were injected subcutaneously with **IL-6** (100-1000 U) or IFN-alpha (1000-10,000 U). On day 46, numbers of CD23+ **lymphocytes** in Peyer's patches (PP), mesenteric lymph nodes (MLN), and spleen and level of soluble CD23 in serum were determined (flow. . . assay, confirmed by competition assay). Data are expressed as percent total cells or as optical density at 490 nm. IFN-alpha **treatment** strongly suppressed up to 100% numbers of CD23+ cells exclusively in PP (i.e., numbers of CD23+ cells in MLN and spleen were unchanged) whereas serum levels of soluble CD23 were dramatically increased (60%). **IL-6 treatment** had no effect on either numbers of CD23+ **lymphocytes** or on serum levels of soluble CD23. The data suggest that the mechanisms by which IFN-alpha, but not **IL-6**, regulates IgE responses involves suppression of CD23 expression on **lymphocytes** in PP and supports a central role for these organs in regulation of IgE responses in vivo.

L4 ANSWER 10 OF 21 MEDLINE

DUPLICATE 10

ACCESSION NUMBER: 00187851 MEDLINE
DOCUMENT NUMBER: 00187851
TITLE: Anti-CD3 monoclonal antibody-induced receptor changes. II. Interaction of CD2 and CD3.
AUTHOR: Lin J; Thavink E D; Qin L; Ding Y; Bronberg J S
CORPORATE SOURCE: Department of Surgery, University of Michigan, Ann Arbor 48109, USA.
CONTRACT NUMBER: A122515 (NIAID)
SOURCE: JOURNAL OF IMMUNOLOGY, (1996 Feb 1) 167 (2) 249-58.
JOURNAL CODE: CD9. ISSN: 0008-8749.
PUB. COUNTRY: United States
JOURNAL: Article; JOURNAL ARTICLE
LANGUAGE: English
FILE SECTENI: Priority Journals; Index Journals
ENTRY MONTH: 199602

AB Anti-CD3 monoclonal **antibodies** (mAbs) and anti-CD2 mAbs each prolong allograft survival and cause transient downmodulation of homologous **receptor** expression. Anti-CD2 mAb also act synergistically with anti-CD3 mAbs to prolong allograft survival and induce tolerance. The effect of combined anti-CD2 and anti-CD3 mAb **treatment** on **receptor** expression was further analyzed with an in vitro model. The anti-CD2 mAb 1E-15 caused CD2 expression on purified splenic T. . . decreasing CD3 expression [69.1% (3.47) to 69.9% (2.37)]. Modulation of CD2 and CD3 expression was similar on mixed splenic T **lymphocytes** and isolated CD4 and CD8 subsets. Modulation did not change with the addition of the cytokines IL-1, IL-2, IL-4, **IL-6**, IL-10, TGF alpha, or TGF beta. Kinetic studies showed that modulation of CD2 was rapid, persistent, and of the same. . . magnitude from Day 1 to Day 7 of culture while CD3 downmodulation was transient. The results of transcriptional analysis and **receptor** distribution suggested that downmodulation was due to **receptor** internalization while upmodulation was due to increased transcription. Analysis of expression of other adhesion molecules demonstrated that CD11b, CD13, CD44, . . . and CD3 expression on T cells

and modulation is accompanied by changes in the array of other T cell surface **receptors**. Changes in cell surface **receptor** display may provide an additional explanation for the synergistic effect of anti-CD2 plus anti-CD3 in prolonging allograft survival.

L4 ANSWER 11 OF 21 MEDLINE

DUPLICATE 11

ACCESSION NUMBER: 9700503 MEDLINE
DOCUMENT NUMBER: 9700503
TITLE: 15-Iscaryspergualin inhibits interleukin 6 production in in vitro stimulated human lymphocytes.
AUTHOR: Eorg A J; Kumagai-Braesch M; Moller E
CORPORATE SOURCE: Department of Immunology, Microbiology, Pathology and . . .

SOURCE: Infectious Diseases, Farolinska Institute, Huddinge Hospital, Sweden.
 TRANSLANT IMMUNOLISY, (1996 Jun) 4 (2) 133-43.
 J. Anal. code: E3L. ISSN: 0966-3274.
 PUB. COUNTRY: ENGLAND: United Kingdom
 J. Anal. Article: (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journal
 ENTRY MONTH: 1-8704

AB Experimental data show that relatively low concentrations of 15-deoxyspergualin (DSG) inhibit the induction of cytotoxic T **lymphocytes** (CTL) and the generation of **antibody**-producing cells. Considerably higher concentrations of DSG are required to inhibit proliferative responses. In this in vitro study, the effects of . . . DSG on CTL induction, on proliferative responses induced by different stimuli, and on the production of interleukins IL-1, IL-2 and IL-6 and IFN-gamma (gamma-interferon) were assessed and compared with the effects of CSA (cyclosporine A) and/or FK506. We confirmed the suppressive . . . the generation of CTL. Quite unexpectedly, however, we found that, although DSG did not affect the proliferative response to allogeneic **lymphocytes** or a superantigen, it did inhibit proliferation of peripheral blood leucocytes (PBL) stimulated with *Staphylococcus aureus*. DSG was active even . . . lower in cells stimulated by *S. aureus* in the presence of DSG, showing a selective effect on CD3-CD4+ responder T **lymphocytes**. The proportion of IL-2 **receptor** (CD25) positive cells was also reduced by DSG **treatment**. Moreover, we found that DSG inhibited the proliferation induced by PHA (phytohemagglutinin) but not by Con A (concanavalin A). Thus, . . . CD3-mediated pathway. DSG did not influence

the production of IL-2 or IFN-gamma or the lipopolysaccharide induced production of IL-2 or IL-6. In contrast, the production of IL-6 was inhibited when cells were stimulated by allogeneic **lymphocytes**, *S. aureus*, PHA or Con A. This suggested that the DSG-suppressed IL-6 production could be the basis for the other observed effects. We tried to mimic the DSG effects with **antibodies** and indeed found that the IL-6 specific **antibodies** had similar effects. Furthermore, recombinant IL-6 completely overcame the suppressive effects of DSG on *S. aureus* and PHA induced proliferation, whereas addition of IL-6 to DSG treated PBL only partly restored the cytotoxic activity of lymphoblasts induced by allogeneic cells. Thus, the inhibitory effect of DSG on de novo synthesis of IL-6 could explain some of its immunosuppressive effects, but additional DSG-sensitive steps are obviously involved in CTL induction and differentiation.

L4 ANSWER 11 OF 21 MEDLINE DUPLICATE 12
 ACCESSION NUMBER: 96117111 MEDLINE
 DOCUMENT NUMBER: 96117111
 TITLE: Selective immunomodulation in patients with inflammatory bowel disease--future therapy or reality?
 AUTHOR: van Hogeand E. A; Verspaget H W
 CORPORATE SOURCE: Department of Gastroenterology-Hepatology, University Hospital Leiden, Netherlands.
 SOURCE: NETHERLANDS JOURNAL OF MEDICINE, (1996 Feb) 48 (2) 64-7. Ref: 21
 J. Anal. code: NWL. ISSN: 0300-2977.
 PUB. COUNTRY: Netherlands
 J. Anal. Article: (JOURNAL ARTICLE)
 General Review: (REVIEW)
 (REVIEW, TUTORIAL)
 LANGUAGE: English
 ENTRY MONTH: 19-703
 ENTRY WEEK: 19-70304
 AB . . . has not so far been elucidated. In theory, an antigen-presenting

cell forms a complex with endotoxin-derived peptides as antigen. T-helper **lymphocytes** recognize this complex, are activated and start to produce cytokines. For inflammatory bowel diseases (IBD) the most important cytokines identified are interleukin 1 (IL-1), interleukin 2 (IL-2), interleukin 6 (IL-6), interleukin 8 (IL-8), gamma-interferon (IFN- γ), and tumor necrosis factor-alpha (TNF-alpha). Inhibition of these cytokines can be achieved by administration of cyclosporine, which inhibits the function of T-helper **lymphocytes**. Orally, intravenously, and locally administered cyclosporine is able to improve the disease activity in ulcerative colitis and Crohn's disease, but... immunosuppressant FK506 has comparable actions to cyclosporine in regulating cytokine production and may even be more effective than cyclosporine. The **receptor** antagonist of IL-1 (IL-1ra) competitively binds to the IL-1 **receptor** located on several **lymphocytes**. **Treatment** of animals with IL-1ra has been successful and clinical trials using recombinant IL-1ra are underway in IBD. **Antibodies** against alphaIL-21 have also been used successfully in animal studies. No experience with this substance has been obtained in man. The use of alpha-interferon seems to be effective in some patients with Crohn's disease. CD4 and CD8 molecules on **lymphocytes** are needed to form the interaction between antigen, antigen-presenting cell, and **lymphocytes**. Specific monoclonal **antibodies** against CD4 are successfully used in patients with active ulcerative colitis and Crohn's disease. TNF-alpha shares many of the proinflammatory activities of IL-1. In preliminary studies, especially in patients with Crohn's disease, the effects of the administration of **antibodies** to TNF-alpha were excellent.

L4 ANSWER 13 OF 21 MEDLINE DUPLICATE 13
 ACCESSION NUMBER: 96152717 MEDLINE
 DOCUMENT NUMBER: 96152717
 TITLE: Antibody-targeted superantigen therapy induces tumor-infiltrating lymphocytes, excessive cytokine production, and apoptosis in human colon carcinoma.
 AUTHOR: Litten M J; Iohlstén H; Lande P A; Halland T; Ohlsson L; Andersson U
 CORPORATE SOURCE: Department of Immunology, Arrhenius Laboratory for Natural Sciences, Stockholm University, Sweden.. mark@imm2.su.se
 SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (1996 Jan) 26 (1) 1-9.
 Journal code: EN5. ISSN: 0014-2936.
 PUB. COUNTRY: GERMANY, Federal Republic of
 Journal: Article; JOURNAL ARTICLE
 LANGUAGE: English
 FILE SEGMENT: Priority Journals; Backed Journals
 ENTRY MONTH: 199605

AB Bacterial superantigens are the most potent known activators of human T **lymphocytes**. To engineer superantigens for immunotherapy of human colon carcinoma, the superantigen, staphylococcal enterotoxin A (SEA) was genetically fused to the Fab region of the colon carcinoma-reactive monoclonal **antibody** C242. In the present study the effector mechanisms involved in the anti-tumor response to C242 Fab-SEA were characterized. Immunohistochemistry and... IL-4, IL-5, IL-10, IL-12, interferon (IFN)-gamma, granulocyte-macrophage colony-stimulating factor, and transforming growth factor-beta, whereas IL-1-alpha, IL-1ra, IL-1 beta, TNF-beta, IL-3, **IL-6**, and IL-8 were undetectable. Most of the TNF-alpha, IL-2, IL-12, and IFN-gamma were made by the infiltrating human leukocytes, while the colon carcinoma cells were induced to produce IL-4, IL-10, and TNF-alpha. Up-regulation of IFN-gamma **receptors** and TNF R p80 **receptors** was found, while the TNF R p80 **receptor** was absent. The cytokine production, T cell infiltration, and CD95 Fas **receptor** expression concomitantly

occurred to induce programmed cell death in the tumor cells. This was followed by a strong reduction of the tumor mass that was seen within 24

h

after C242 Fab-SHA infusion. These findings demonstrate that **antibody**-superantigen proteins efficiently recruit tumor-infiltrating **lymphocytes** actively producing a variety of cytokines likely to be essential for the therapeutic effects observed in the model. Although the humanized SCID model has obvious limitations in its predictive value for **treatment** of human cancer, we believe that these results encourage clinical evaluation of **antibody**-targeted superantigens.

L4 ANSWER 14 OF 21 MEDLINE

DUPLICATE 14

ACCESSION NUMBER: 95193051 MEDLINE
DOCUMENT NUMBER: 95193051
TITLE: CD38 ligation induces discrete cytokine mRNA expression in tumor cultured lymphocytes.
AUTHOR: Lucifora C M; Urbani F; La Sala A; Funaro A; Malavasi F
CORPORATE SOURCE: Laboratorio di Batteriologia e Malologia Medica, Istituto Superiore di Sanita, Roma, Italy.
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (1995 May) 25 (5) 1477-80.
Journal code: EN5. ISSN: 0014-2980.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199509

AB Human CD38 is a surface glycoprotein expressed by different immune-competent cells such as immature and activated **lymphocytes**, plasma cells and natural killer cells. It has recently been reported that the CD38 molecule exerts adenosine diphosphate ribosyl cyclase activity and is associated with distinct transmembrane signaling molecules. This study reports that ligation of CD38 by specific monoclonal

antibodies (mAb) induces multiple cytokine mRNA expression in cultured peripheral blood mononuclear cells (PBMC). The mRNA for tumor necrosis factor-alpha, interleukin (IL-1 beta, IL-6, granulocyte-macrophage colony-stimulating factor (GM-CSF) and IL-12 were always detected, whereas interleukin-gamma and IL-2 mRNA expression were seen in most, but . . . between CD38 and CD3 activation are the low to undetectable levels of IL-2 mRNA, and the sustained IL-1 beta and IL-6 mRNA accumulation found in PBMC cultures following **treatment** with anti-CD38 mAb. Furthermore, PBMC proliferation was not found to be a prerequisite for CD38-mediated cytokine induction. Together, these results. . . induction of a discrete array of cytokines, and that this pathway only partially overlaps with that controlled by T cell **receptor** CD3.

L4 ANSWER 15 OF 21 MEDLINE

DUPLICATE 15

ACCESSION NUMBER: 95250171 MEDLINE
DOCUMENT NUMBER: 95250171
TITLE: Anti-CD2 monoclonal antibody-induced receptor changes: down
modulation of cell surface CD2.
AUTHOR: Lin J; Von E W; Chavan P L; Qin L; Woodward J; Ding Y; Yagita H; Bromberg J S
CORPORATE SOURCE: Department of Microbiology, Medical University of South Carolina, Charleston 29425, USA..
CONTRACT NUMBER: A1336 S (NIAID)
SOURCE: TRANSPLANTATION, (1995 Apr 27) 59 (8) 1162-71
Journal code: WE1. ISSN: 0014-1337.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199508

AB . . . LFA-1 beta (CD18), Pgp-1 (CD44), CD45, MEL-14 (L-selectin), and VLA-4 alpha (CD49a), were all increased as a result of anti-CD2 treatment, whereas CD25 (IL-2R), CD48 (CD2 ligand), and ICAM-1 (CD54) remained unchanged. Kinetics showed that CD2 down-modulation was persistent and at . . . from day 1 through day 7 of culture. Anti-CD2 mAb could down modulate CD2 on both CD4 and CD8 splenic **lymphocyte** subsets, thymocytes, and the T cell lymphoma EL-4; and, non-T cells did not seem to participate in the process of. . . of T cell CD2 expression

in an epitope and isotype dependent fashion and that CD2 down-modulation correlated with inhibition of **receptor**-driven T cell stimulation. Inter-**antibody**, including the Fc portion, was required to induce CD2 down-modulation, and additional experiments suggested an interaction with an Fc gamma. . . Fc gamma RII or Fc gamma

RIII. CD2 down-modulation did not change with the addition of the cytokines IL-1, IL-2, IL-6, IL-10, TNF alpha, or TGF-beta 1. These results show that anti-CD2 mAbs significantly and persistently down-modulate CD2 on various T cell subpopulations. The mAbs must interact with both the CD2 **receptor** and in Fc gamma R. CD2 down-modulation is accompanied by changes in the array of other T cell surface **receptors** that may contribute to mechanisms of anti-CD2-induced immunosuppression.

L4 ANSWER 16 OF 21 MEDLINE

ACCESSION NUMBER: 199-09495 MEDLINE

DOCUMENT NUMBER: 9402921

TITLE: Clinical and immunological follow-up of patients with AIDS-associated Kaposi's sarcoma treated with an anti-IL-6 monoclonal antibody.

AUTHOR: Rocard E; Audray E; Davenney H; Thyss A; Lang J M; Willems J; Herve F

CORPORATE SOURCE: Centre de Transfusion Sanguine, Besancon, France.

SOURCE: CYTOKINES AND MOLECULAR THERAPY, (1995 Jun) 1 (2) 133-8. Journal code: CNL. ISSN: 1355-0568.

PUB. COUNTRY: ENGLAND; United Kingdom

(CLINICAL TRIAL
Journal; Article; JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199506

ENTRY WEEK: 1995234

AB . . . in stage III B and one in stage IV of the disease) were treated for 14 days with E-Fc, an anti-IL-6 monoclonal **antibody** (IgG1), at a daily dose of 10 mg. No side-effects were observed, but no patients experienced a complete or partial response. No modification was noted in the analysis of **lymphocyte** subsets, except for a transient decline in the number of cells expressing CD36, accompanied by altered NK activity in four of the seven evaluable patients. Anti-IL-6 mAb prevented the binding of IL-6 to its cell membrane **receptor**, as documented by the decline in C reactive protein levels. However, anti-IL-6 mAb induced the circulation of significant amounts of IL-6, probably in the form of monomeric immune complexes. The sera, analysed on B9 cell line, demonstrated a stimulating activity, indicating that hypersensitive cells were able to cleave these complexes. This observation, together with the clinical inefficacy of the **treatment**, should prompt us to be careful with the use of unmanipulated single monoclonal **antibodies**, especially in cancer patients.

L4 ANSWER 17 OF 21 MEDLINE

DUPLICATE 16

ACCESSION NUMBER: 9402921 MEDLINE

DOCUMENT NUMBER: 9402921

TITLE: Combination anti-CD2 and anti-CD3 monoclonal antibodies induce tolerance while altering interleukin-2,

interleukin-4, tumor necrosis factor, and transforming growth factor-beta production.

AUTHOR: Charvin K D; Qin L; Lin J; Woodward J E; Baliga P; Bromberg J S

CORPORATE SOURCE: Department of Surgery, Medical University of South Carolina, Charleston..

CONTRACT NUMBER: A132655 (NIH-10)

SOURCE: ANNALS OF SURGERY, (1993 Oct) 218 (4) 492-501; discussion 501-..

PUB. COUNTRY: Journal code: 67S. ISSN: 0003-4932. United States

LANGUAGE: Journal; Article; (JOURNAL ARTICLE) English

FILE SEGMENT: Abstracs; Index Medicus Journals; Priority Journals; Cancer Journals

ENTRY MONTH: 1994 1

AB OBJECTIVE: These studies were designed to elucidate the mechanism by which signals delivered by anti-CD2 monoclonal **antibody** (MoAb) interfere with activation signals delivered by anti-CD3 MoAb and induce long-term graft survival and tolerance. SUMMARY BACKGROUND DATA: Anti-CD2.

. . . anti-CD2 and/or anti-CD3 MoAbs intravenously only at the time of initial allografting. Serum from treated animals and culture supernatants from **lymphocytes** stimulated in vitro with anti-CD3 were examined for interleukin IL-2, -4, -6, and -10, tumor necrosis factor (TNF), and transforming growth factor-beta (TGF beta). RNA was isolated from **lymphocytes** from treated animals and examined for **receptor** and cytokine gene expression by northern hybridization or reverse transcribed and amplified by the polymerase chain reaction (PCR).

RESULTS: Anti-CD2. . . toxicity. Second donor-specific allografts also showed long-term survival. The peak serum TNF concentration (2100 units/mL) was reduced 78% by anti-CD2 **treatment** (455 units/mL). Anti-CD2 inhibited anti-CD3-stimulated proliferation and in vitro production of IL-2 and IL-4, with no alteration of IL-6, IL-10, or TNF. Conversely, there was an increase in the immunosuppressive cytokine TGF beta. PCR analysis showed that anti-CD2 reduced. . . IL-2

messenger RNA expression, and by northern analysis, anti-CD2 inhibited anti-CD3-stimulated increases in messenger RNA for the CD2 and CD3 **receptors** themselves. CONCLUSIONS: The combination of anti-CD2 and anti-CD3 MoAbs induced a state of tolerance while decreasing anti-CD3-associated cytokine toxicity. The. . .

L4 ANSWER 18 OF 21 MEDLINE DUPLICATE 17

ACCESSION NUMBER: 9434609 MEDLINE

DOCUMENT NUMBER: 9434609

TITLE: Characterization of unique lymphoid cells derived from murine spleen which constitutively produce interleukin-6.

AUTHOR: O'Neill R C; Nal F

CORPORATE SOURCE: Division of Clinical Sciences, John Curtin School of Medical Research, Australian National University, Canberra, Australia..

SOURCE: IMMUNOCY, 1993 Jun) 79 (2) 220-8. Journal code: G81. ISSN: 0019-2805.

PUB. COUNTRY: ENGLAND: United Kingdom

LANGUAGE: Journal; Article; (JOURNAL ARTICLE) English

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 199311

AB . . . stimulation was used to expand the lymphoid cells remaining in spleen following depletion of CD4+ and CD8+ T cells by **antibody** and complement **treatment**. Cells were cultured in the presence of concanavalin A (Con A), interleukin-2 (IL-2) and syngeneic irradiated

spleen feeder cells. This. . . unique to T, B or myeloid cells. All cell lines represent agranular lymphoblasts and show no evidence of early T-cell **receptor** (TCR) or Ig heavy chain gene rearrangements, suggesting no commitment to T-or B-lymphoid lineage. Despite expression

of

the NK1.1 marker. . . factor-alpha (TNF-alpha) or granulocyte-macrophage colony-stimulating factor (GM-CSF) in cell supernatants. However, all but one of these cell lines constitutively produce IL-6. Each cell line has been shown to induce T-cell proliferation independently in mixed **lymphocyte** reactions, implicating the capacity of these cells to act as antigen-presenting cells. Consistent with this hypothesis is the observation that. . .

L4 ANSWER 19 OF 21 MEDLINE

DUPLICATE 18

ACCESSION NUMBER: 013 017 MEDLINE

DOCUMENT NUMBER: 013 017

TITLE: Enhancement of lymphokine-activated T killer cell tumor necrosis factor receptor mRNA transcription, tumor

necrosis

factor receptor membrane expression, and tumor necrosis factor/lymphotoxin release by IL-1 beta, IL-4, and IL-6 in vitro.

AUTHOR: Dent C A; Gatanaga M; Inhans E K; Cappuccini F; Yamamoto R S; Branger S A; Gatanaga T

CORPORATE SOURCE: Department of Molecular Biology & Biochemistry, University of California Irvine 92717..

SOURCE: JOURNAL OF IMMUNOLOGY, (1991 Mar 1) 146 (5) 1522-6.

Journal code: JIM. ISSN: 0022-1767.

PUB. COUNTRY: United States

Journal Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abstract; Index Medicus Journals; Priority Journals; Cancer Journals

ENTRY MONTH: 199103

AB Co-culture with IL-2 can induce human T **lymphocytes** to proliferate and become nonphenotypically restricted, lymphokine-activated killer (LAK) cells in vitro. Our studies were conducted with long term cultured, . . . CD3+. We found that proliferating 7 to 10-day human T-LAK cells express TNF, by using a 125I-TNF binding assay. Additional **treatment** of these cells with the cytokines IL-1 beta, IL-4, or IL-6 rapidly up-regulated IL-2/IL-3 TNF mRNA transcription and doubled TNF membrane expression. Further studies revealed that these cytokines also increased the release of TNF and lymphotoxin (LT). **Antibody** neutralization studies indicated that IL-1 induces release of both TNF and LT; however, IL-4 and IL-6 induce primarily LT release. These results further support the concept that these cytokines are involved in the regulation of TNF/LT release, TNF synthesis, and TNF membrane expression. It is apparent that cytokines and their membrane **receptors** are involved in the autocrine/paracrine control of T cell proliferation, differentiation, and expression of functional activity after IL-2 stimulation in. . .

L4 ANSWER 20 OF 21 MEDLINE

DUPLICATE 19

ACCESSION NUMBER: 92180773 MEDLINE

DOCUMENT NUMBER: 92180773

TITLE: Tissue-specific homing receptor mediates lymphocyte adhesion to cytokine-stimulated lymph node high

endothelial

venule cells

AUTHOR: Chin J Y; Cal J F; Xu X M

CORPORATE SOURCE: Department of Microbiology and Immunology, University of Miami School of Medicine, Florida 33101..

CONTRACT NUMBER: AI 25140 (NIAID)

SOURCE: IMMUNOLOGY, (1991 Nov) 74 (3) 478-83.

Journal code: GIM. ISSN: 0019-2805

PUB. COUNTRY: ENGLAND: United Kingdom

Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199204

AB **Lymphocytes** bind to high endothelial venule (HEV) cells as the first step in the migration of these cells into lymph nodes. . . and cultured HEV cells from rat LN and investigated the effects of cytokines on the adhesiveness of these cells for **lymphocytes**. The results showed that **lymphocytes** from thoracic duct, spleen and LN adhered preferentially to the cultured LN HEV cells compared to cells isolated from the thymus and bone marrow. The adhesiveness of LN HEV cells for thoracic duct **lymphocytes** (TDL) was significantly increased in a dose- and time-dependent manner by pretreatment of the HEV cells with tumour necrosis factor-alpha (TNF-alpha), interferon-gamma (IFN-gamma) or interleukin-4 (IL-4). In contrast, pretreatment of HEV cells with IL-1, IL-6 or IL-7 did not alter the capacity of LN HEV cells to adhere **lymphocytes**. Furthermore, incubation of LN HEV cells with suboptimal doses of INF and IL-1, IFN-gamma and IL-4, or TNF-alpha and IFN-gamma. . . to increase the adhesiveness. The adhesion of TDL to non-stimulated and IL-4-stimulated LN HEV cells could be blocked specifically by treatment of **lymphocytes** with the LN homing-receptor-specific A.11.5 monoclonal antibody (mAb). In contrast, **lymphocytes** pretreated with the PP-homing receptor-specific B3.1.6 mAb or the antileucocyte common antigen (LX1) mAb adhered normally to the HEV cells. Taken together, these results indicate that the baseline and cytokine-stimulated bindings between **lymphocytes** and LN HEV cells are mediated by adhesive mechanisms that regulate **lymphocyte** migration into LN in vivo and provide strong evidence that cytokines are central mediators of organ-specific **lymphocyte** migration.

L4 ANSWER 21 OF 21 BIOSIS (COPYRIGHT 2000) BIOSIS DUPLICATE 20
ACCESSION NUMBER: 1989:41869 BIOSIS
DOCUMENT NUMBER: BA88:87956
TITLE: FUNCTIONAL AND MOLECULAR CHARACTERIZATION OF B CELL LINE DERIVED INTERLEUKIN-1-ALPHA.
AUTHOR(S): VYTH-IEEESE P A; HUKMAN A; WIJFFELS J; GEERTSMA M; DELEENEN J A M; BOSDA J; MEIJER J J M; BERTOLIO F
CORPORATE SOURCE: DIV. IMMUNOL, NETHERLANDS CANCER INST., PLESMANLAAN 121, 1066 CX AMSTERDAM, THE NETHERLANDS.
SOURCE: LEUKEMIA (BALTIMORE), 1989) 3 (8), 585-592.
CODEN: LEUHEB. ISSN: 0732-3794.
FILE SEGMENT: BA; CII
LANGUAGE: English

AB. . . supernatant from STS 15 cells (STS 25 SUP) does not show activity in assays for interleukin-2 (IL-2), -4 (IL-4), -6 (IL-6), interferon or tumor necrosis factor, but is active in the thymocyte costimulation assay and the D10.G4.1 T helper clone proliferative. . . The IL-1 character of the STS 25 SUP activity was confirmed in inhibition studies with three different poly-or monoclonal anti-IL-1 antibodies (31, 88, and 94% inhibition in thymocyte costimulation assay, respectively). Furthermore, complete blocking of D10.G4.1 cell proliferation mediated by STS 25 SUP was observed by including anti-IL-1.alpha. specific antibody in the assay, whereas anti-IL-1.beta. antibody had no effect. These results indicate that this STS 25 SUP activity can be attributed to the presence of IL-1.alpha. . . constitutive expression of IL-1.alpha. messenger RNA by STS 25 cells. In contrast, no IL-1.beta. message was detectable, not even after treatment of the cells with phorbol ester of cycloheximide, which resulted in approximately 5-fold enhancement of IL-1.alpha. mRNA

expression. Binding studies with radiolabeled recombinant (r) IL-1.alpha. indicated the presence of high numbers of IL-1 **receptors** on STS 25 cells (1,170 per cell, $K_d = 392$ pM). Although both IL-1.alpha. and IL-1.beta. bound to these IL-1 **receptors**, no indication was found for IL-1 mediated regulation of STS 25 cell growth. STS 25 SUP as well as rIL-1.alpha. were comparably active in enhancing mitogen stimulated proliferation and/or Ig secretion by normal peripheral blood T **lymphocytes** or normal tonsil B **lymphocytes**. Moreover, STS 25 SUP and rIL-1.alpha., but not recombinant granulocyte/macrophage colony stimulating factor (rGM-CSF), enhanced the proliferation in 1/8 and. . . .

=> s (il-6 (a) receptor) (s) antibody (p) lymphocyte (p) treatment

L5 0 (IL-6 (A) RECEPTOR) (S) ANTIBODY (P) LYMPHOCYTE (P) TREATMENT

=> log y

COST IN U.S. DOLLARS

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TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

45.43

45.64

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